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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,634	10/27/2003	Jun Tan	12062.105020	2636

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KING & SPALDING
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-4003

EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
08/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/694,634	TAN ET AL.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7 and 93-120* is/are pending in the application.

4a) Of the above claim(s) *5,7 and 97-106* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,93,96 and 107-120* is/are rejected.

7)☒ Claim(s) *108* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

2. Claims 2 and 8-92 have been cancelled. Claims 1, 3, and 4 have been amended. Claims 5-7 have been withdrawn from consideration for being drawn to nonelected invention or species. Claims 94-120 are new. Since the new claims 97-106 are drawn to non-elected species, they are withdrawn from further consideration.

Claims 1, 3, 4, 93, 96, and 107-120 are under examination.

3. All rejection pertaining to claims 2, 8, 16, 19, and 20 are moot because Applicant cancelled the claims in the response filed on 05/29/2007.

Specification

3. The claim listing is objected to because it does not indicate the proper status of claims 5-7. Claims 5-7 are identified as "withdrawn", while the correct identifier is "withdrawn and currently amended". Appropriate correction is required.

The following is a citation from MPEP 714[R-3] - Amendments, Applicant's Action

37 CFR 1.121. Manner of making amendments in application.

c) Claims . Amendments to a claim must be made by rewriting the entire claim with all changes (e.g., additions and deletions) as indicated in this subsection, except when the claim is being canceled. Each amendment document that includes a change to an existing claim, cancellation of an existing claim or addition of a new claim, must include

a complete listing of all claims ever presented, including the text of all pending and withdrawn claims, in the application. The claim listing, including the text of the claims, in the amendment document will serve to replace all prior versions of the claims, in the application. In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered).

Response to Arguments

Double Patenting

4. Applicant has requested that the obvious-type double patenting rejections set forth by the Examiner be held in abeyance. The Applicants' comments are acknowledged, however the rejections will be maintained until a Terminal Disclaimer is filed or claims are amended to obviate the rejection.

Claim Rejections - 35 USC § 112, 2nd paragraph

5. The rejections of claims 1, 3, and 4 under 35 U.S.C. 112, second paragraph, as being indefinite or for being incomplete are withdrawn in response to Applicant's amendment to the claims filed on 05/29/2007.

Claim Rejections - 35 USC § 102

6. The rejection of claims 1, 3, and 4 under 35 U.S.C. 102(b) as being anticipated by Tan et al. is withdrawn in response to Applicant's amendment to the claims filed on 05/29/2007.

7. The rejection of claim 1 under 35 U.S.C. 102(e) as being anticipated by Force et al. (PGPUB 2003/0059427) is withdrawn in response to Applicant's amendment to the claims filed on 05/29/2007.

Claim Rejections - 35 USC § 103

8. The rejection of claims 1, 3, and 4 under 35 U.S.C. 103(a) as being unpatentable over either Tan et al., as applied to claims 1-4, in view of both Zheng et al. (PGPUB 2004/0067982) and Gerritse et al. (Proc Natl Acad Sci USA, 1996, 93: 2499-2504) is withdrawn in response to Applicant's amendment to the claims filed on 05/29/2007.

9. The rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Force et al., in view of both Zheng et al. and Gerritse et al. is withdrawn in response to Applicant's amendment to the claims filed on 05/29/2007.

New Rejections/Objections

Claim Objections

10. Claim 108 is objected to because of the following informalities: the claim discloses an antibody that "agonizes" CD40L activity. It is noted that "to agonize" means to suffer or to make a great effort, and, most probably, this is not what Applicant wants to claim. Appropriate correction is required.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 93, and 110-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Force et al. (PGPUB 2003/0059427, of record), in view of Tan et al. (EMBO J, February 25, 2002, 21: 643-652, Applicant's IDS).

Force et al. teach a method of screening the ability of antibodies directed against CD40R to interfere with the CD40L/CD40R signaling pathway by contacting cells that express CD40R with the antibodies to be tested in the absence or presence of CD40L and measuring the level of CD95 expression (i.e., measuring the level of a marker) (p. 3, paragraph 0029, p. 17, paragraph 0176, and Fig. 3). Therefore, Force et al. teach a method of screening the ability of compounds to interfere with the CD40L/CD40R signaling pathway, upstream of CD40L/CD40R interaction, by (i) contacting a first sample of cells with CD49L and measuring the level of a marker, (ii) contacting a second sample of cells with a compound and CD40L, and measuring the level of the same marker, and (iii) comparing the level of the marker in the first sample with the level of the same marker in the second sample (claims 1 and 93). Force et al. do not teach using neuronal cells in their assay (claim 1). However, it is noted that the claims are directed to an *in vitro* method of screening for compounds that inhibit CD40L/CD40R signaling pathway by using cells expressing CD40R, therefore, one of skill in the art would have known that the use of any cell expressing CD40 would have yielded

predictable results, i.e., identification of compounds that inhibit CD40L/CD40R signaling pathway. Applicant did not provide any evidence that the specific use of neuronal cells (claims 1, 97, and 98) or of neuronal cell derived from a specific source (claims 110-120) would result in unexpected results. Just because Applicant uses another cell type does not render the claims innovative over the prior art. Moreover, it is noted that the prior the prior art teaches that neuronal cells express CD40R (see Tan et al., Abstract, p. 644, columns 1 and 2, p. 645, column 2). One of skill in the art would have known that the substitution of one cell for another cell would render the claimed results and would have known that neuronal cells could also be successfully employed in the claimed screening assay. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

13. Claims 1, 93, and 107-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Force et al. taken with Tan et al. (Science, 1999, 286: 2352-2355, of record), in further view of Gerritse et al. (Proc Natl Acad Sci USA, 1996, 93: 2499-2504, of record)

The teachings of Force et al. and Tan et al. are applied as above for claims 1, 93, and 110-120. Force et al. and Tan et al. do not teach screening for a compound that binds to CD40L (claims 94, 96, and 107-109). However, the prior art teaches the advantage of screening for compounds that target CD40L. For example, Gerritse et al. teach that CD40L has advantages over the constitutively and widely expressed CD40R as a target for intervention because its transient expression is restricted to $CD4^+$ T cells,

which allows targeting of only those T cells actively participating in the response, without affecting the population of T cells at large (p. 2504, column 1). Based on these teachings, one of skill in the art would have been motivated to modify the method of Force et al. and Tan et al. by screening for antibodies that interfere with the CD40R/CD40L signaling pathway by binding to CD40L and would have been expected to have a reasonable expectation of success in using such a method because the art teaches the successful use of such methods to identify compounds with the ability of modulating the CD40L/CD40R signaling pathway. It is noted that by doing such, one of skill in the art would have necessarily identified agonistic and antagonistic antibodies (claims 108 and 109) and antibodies that would decrease CD40L trimerization (claim 96). Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

14. Claims 1, 3, 4, 93, and 107-120 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tan et al. (Science, 1999, 286: 2352-2355, of record), in view of Gerritse et al.

Tan et al. teach a method for testing the ability of monoclonal antibodies directed against CD40R to interfere with the CD40L/CD40R signaling pathway after treatment with $A\beta_{1-42}$ (it is noted that treatment with $A\beta_{1-42}$ is used to induce expression of CD40R on microglia, which otherwise do not express or express very low amounts of CD40R), the method comprising: (i) contacting a first sample of microglial cells (i.e., central nervous system cells) with CD49L and measuring the level of the produced TNF-α, (ii)

contacting a second sample of microglial cells with $A\beta_{1-42}$ and CD40L, and measuring the level of the produced TNF-α, and (iii) comparing the level of TNF-α in the first sample with the level of TNF-α in the second sample (claims 1, 3, 4, and 93) (p. 2353, columns 1 and 2 ; Fig. 4).

Tan et al. do not teach using neuronal cells in their assay (claim 1). However, it is noted that the claims are directed to an *in vitro* method of screening for compounds that inhibit CD40L/CD40R signaling pathway by using cells expressing CD40R, therefore, one of skill in the art would have known that the use of any cell expressing CD40 would have yielded predictable results, i.e., identification of compounds that inhibit CD40L/CD40R signaling pathway. Applicant did not provide any evidence that the specific use of neuronal cells (claims 1, 97, and 98) or of neuronal cell derived from a specific source (claims 110-120) would result in unexpected results. Just because Applicant uses another cell type does not render the claims innovative over the prior art. Moreover, it is noted that the prior the prior art teaches that neuronal cells express CD40R (see Tan et al., Abstract, p. 644, columns 1 and 2, p. 645, column 2). One of skill in the art would have known that the substitution of one cell for another cell would render the claimed results and would have known that neuronal cells could also be successfully employed in the claimed screening assay.

Tan et al. do not teach testing agents that bind CD40L (claims 94, 96, and 107-109). However, the prior art teaches the advantage of screening for compounds that target CD40L. For example, Gerritse et al. teach that CD40L has advantages over the constitutively and widely expressed CD40R as a target for intervention because its

transient expression is restricted to $CD4^+$ T cells, which allows targeting of only those T cells actively participating in the response, without affecting the population of T cells at large (p. 2504, column 1). Based on these teachings, one of skill in the art would have been motivated to modify the method of Tan et al. by screening for antibodies that interfere with the CD40R/CD40L signaling pathway by binding to CD40L and would have been expected to have a reasonable expectation of success in using such a method because the art teaches the successful use of such methods to identify compounds with the ability of modulating the CD40L/CD40R signaling pathway. It is noted that by doing such, one of skill in the art would have necessarily identified agonistic and antagonistic antibodies (claims 108 and 109) and antibodies that would decrease CD40L trimerization (claim 96).

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

Joe Woitach
AU1633